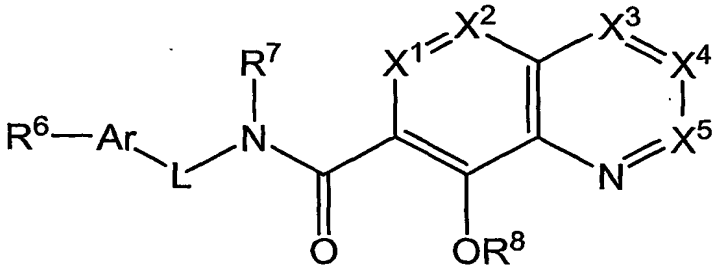
CLAIMS:

1. A compound having the formula:



or a pharmaceutically acceptable salt thereof, and including enol and tautomeric resonance isomers;

wherein:

X^1 is CR^1, NR, or N;

X^2 is CR^2, NR, or N;

X^3 is CR^3, NR, or N;

X^4 is CR^4, NR, or N;

X^5 is CR^5, NR, or N;

at least one of X^1, X^2, X^3, X^4, and X^5 is NR or N;

R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are independently selected from H, F, Cl, Br, I, OH, amino ($-NH_2$), ammonium ($-NH_3^+$), alkylamino, dialkylamino, trialkylammonium, C_1-C_8 alkyl, C_1-C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1-C_8 alkylsulfonate, C_1-C_8 alkylamino, 4-dialkylaminopyridinium, C_1-C_8 alkylhydroxyl, C_1-C_8 alkylthiol, alkylsulfone ($-SO_2R$), arylsulfone ($-SO_2Ar$), arylsulfoxide ($-SOAr$), arylthio ($-SAr$), sulfonamide ($-SO_2NR_2$), alkylsulfoxide ($-SOR$), formyl ($-CHO$), ester ($-C(=O)OR$), amido ($-C(=O)NR_2$), 5-7 membered ring lactam, 5-7 membered ring lactone, nitrile ($-CN$), azido ($-N_3$), nitro ($-NO_2$), C_1-C_8 alkoxy ($-OR$), C_1-C_8 alkyl, C_1-C_8 substituted alkyl, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, C_2-C_{20} heteroaryl, and C_2-C_{20} substituted heteroaryl, phosphonate, phosphate, polyethyleneoxy, and a prodrug moiety; or when X^1 is CR^1 and when X^2 is CR^2, then CR^1 and CR^2 together may form a ring; when X^3 is CR^3 and when X^4 is CR^4, then CR^3 and CR^4 together may form a ring; or when. X^4 is CR^4

and X^5 is CR^5, then CR^4 and CR^5 together may form a ring; wherein the ring is 5, 6, or 7-membered;

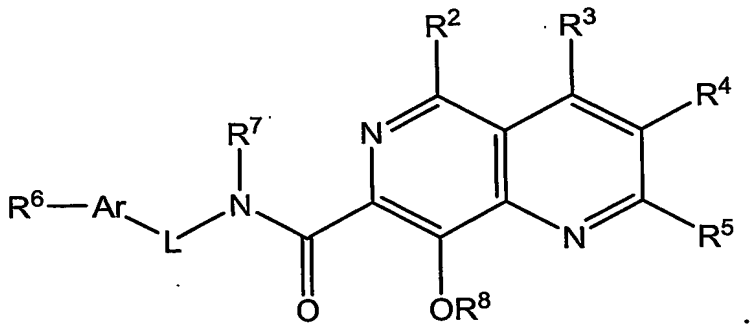
R is independently selected from H, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl;

L is selected from a bond, O, S, NR, N–OR, C_1–C_{12} alkylene, C_1–C_{12} substituted alkylene, C_2–C_{12} alkenylene, C_2–C_{12} substituted alkenylene, C_2–C_{12} alkynylene, C_2–C_{12} substituted alkynylene, C(=O)NH, C(=O), $S(=O)_2$, $C(=O)NH(CH_2)_n$, and $(CH_2CH_2O)_n$, where n may be 1, 2, 3, 4, 5, or 6; and

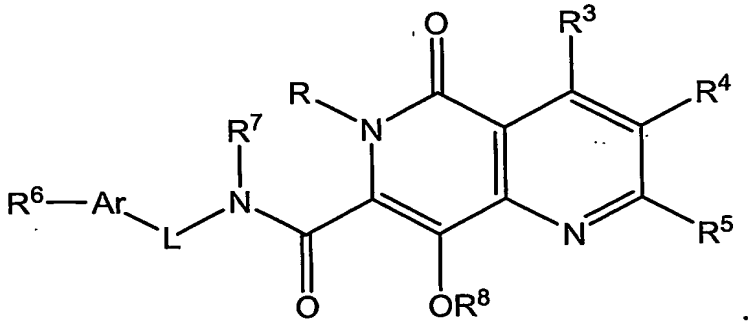
Ar is covalently attached to L and to one or more R^6 and Ar is selected from C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl;

where at least one of R, R^1, R^2, R^3, R^4, R^5, R^6, $R^7$and R^8 comprises a phosphonate group.

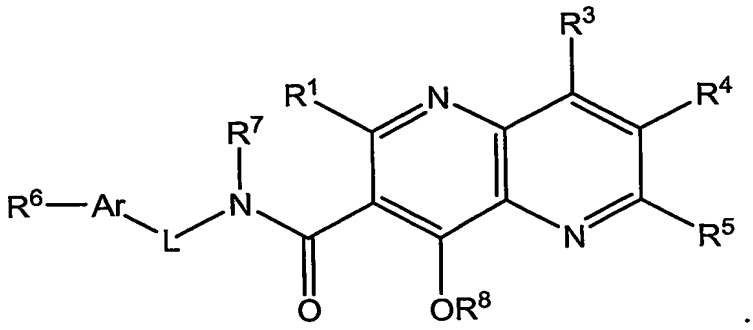
2. A compound according to claim 1 having the formula:



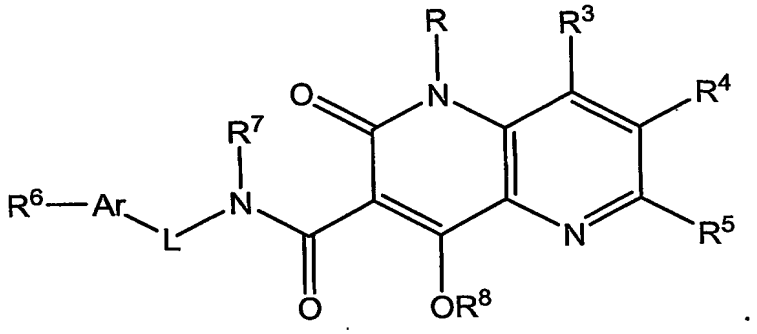
3. A compound according to claim 1 having the formula:



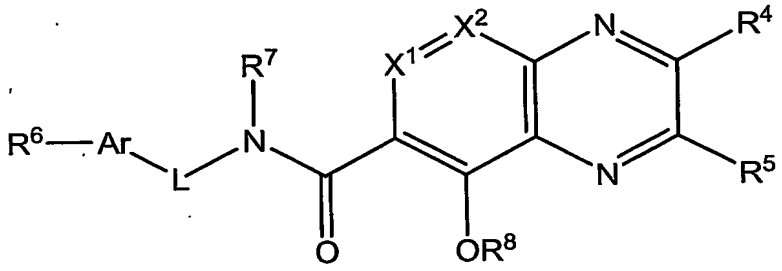
4. A compound according to claim 1 having the formula:



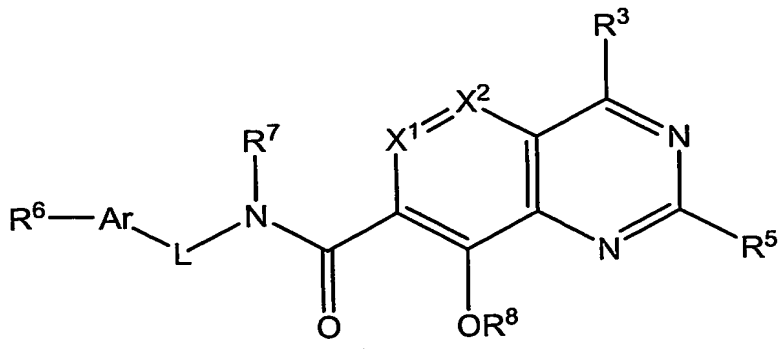
5. A compound according to claim 1 having the formula:



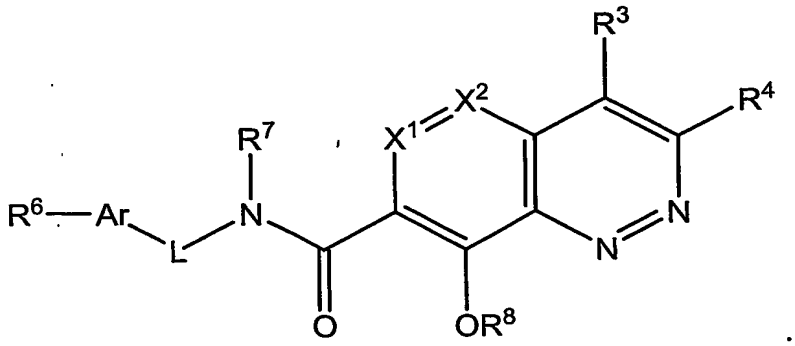
6. A compound according to claim 1 having the formula:



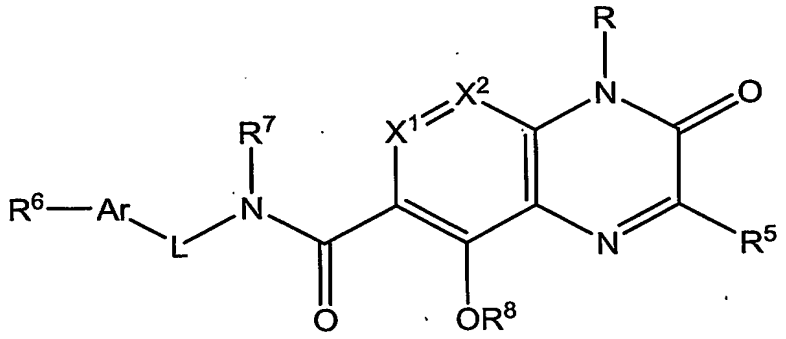
7. A compound according to claim 1 having the formula:



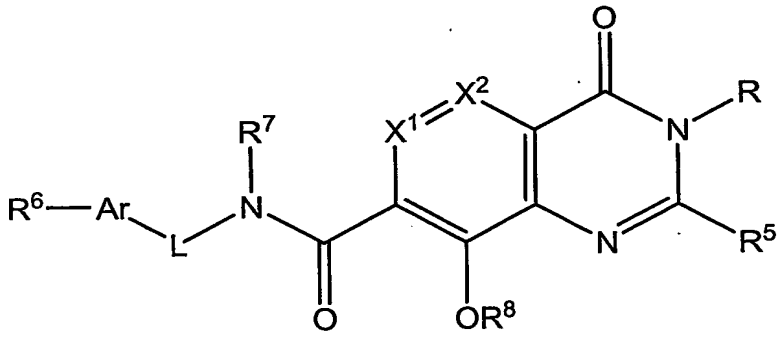
8. A compound according to claim 1 having the formula:



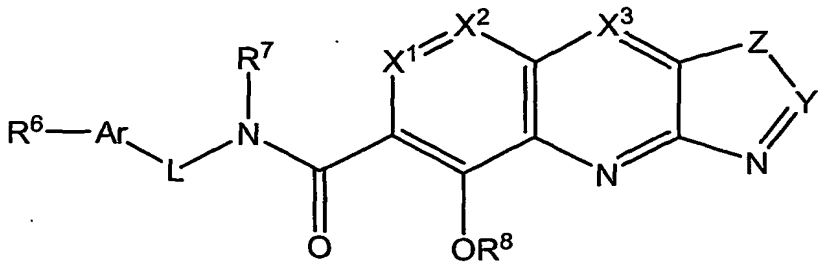
9. A compound according to claim 1 having the formula:



10. A compound according to claim 1 having the formula:



11. A compound according to claim 1 having the formula:



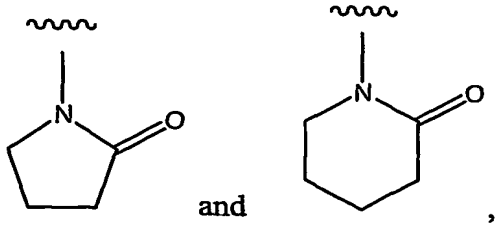
wherein

Y is CR^5, NR or N; and

Z is selected from O, S, NR, CR_2, CROR, CROC(=O)R, C(=O), C(=S), CRSR, $C(=NR_2)$, $C=CR_2$, $CR_2–CR_2$, CR=CR, NR–CR_2, N=CR, N=N, SO_2–NR, $C(=O)CR_2$, $S(=O)CR_2$, SO_2CR_2, C(=O)NR, $CR_2–CR_2–CR_2$, CR=CR–CR_2, CRC(=O)NR, $CR_2SO_2CR_2$, CR_2SO_2NR, CRC(=S)NR, CR=N–CR_2, CR=N–NR, or N=CR–NR.

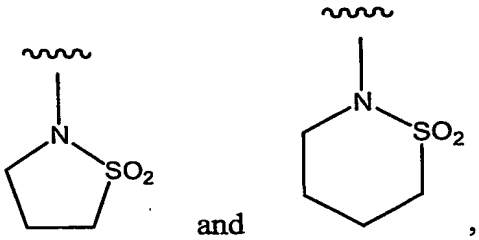
12. The compound of claim 1 wherein substituted alkylene, substituted alkenylene, substituted alkynylene, substituted aryl, and substituted heteroaryl are independently substituted with one or more substituents selected from F, Cl, Br, I, OH, amino ($–NH_2$), ammonium ($–NH_3^+$), alkylamino, dialkylamino, trialkylammonium, $C_1–C_8$ alkyl, $C_1–C_8$ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, $C_1–C_8$ alkylsulfonate, $C_1–C_8$ alkylamino, 4-dialkylaminopyridinium, $C_1–C_8$ alkylhydroxyl, $C_1–C_8$ alkylthiol, alkylsulfone ($–SO_2R$), arylsulfone ($–SO_2Ar$), arylsulfoxide (–SOAr), arylthio (–SAr), sulfonamide ($–SO_2NR_2$), alkylsulfoxide (–SOR), ester (–C(=O)OR), amido ($–C(=O)NR_2$), 5-7 membered ring lactam, 5-7 membered ring lactone, nitrile (–CN), azido ($–N_3$), nitro ($–NO_2$), $C_1–C_8$ alkoxy (–OR), $C_1–C_8$ alkyl, $C_1–C_8$ substituted alkyl, $C_6–C_{20}$ aryl, $C_6–C_{20}$ substituted aryl, $C_2–C_{20}$ heteroaryl, and $C_2–C_{20}$ substituted heteroaryl, phosphonate, phosphate, polyethyleneoxy, and a prodrug moiety.

13. A compound of claim 1 wherein X^2 is CR^2 and R^2 is selected from H, OH, OC(=O)OR, $OC(=O)NR_2$, OC(=O)R, OSO_2NR_2 (sulfamate), NR_2, $NRSO_2R$, SR, S(O)R, SO_2R or SO_2NR_2 (sulfonamide), lactam having the structures:



and ,

sultam having the structures:

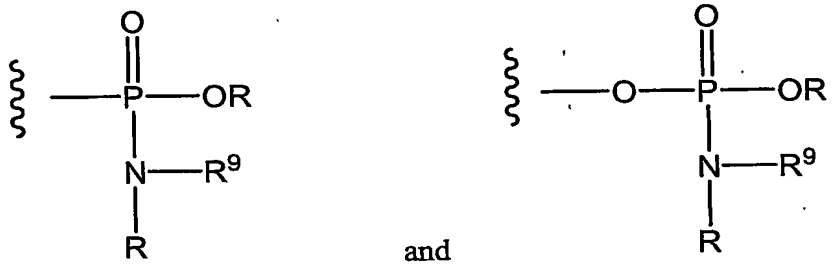


and a prodrug moiety.

14. The compound of claim 1 wherein L is CH_2 and Ar is substituted phenyl.

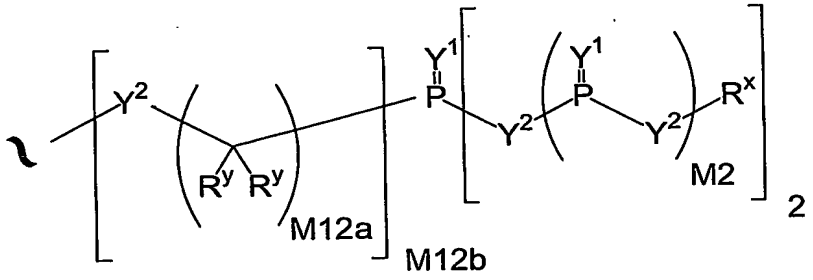
15. The compound of claim 1 where L is CH_2 and Ar is 4-fluorophenyl.

16. The compound of claim 1 wherein at least one of R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 comprise a prodrug moiety selected from the structures:



wherein R^9 is comprised of an ester, an amide, or a carbamate.

17. The compound of claim 1 wherein the phosphonate group has the structure:



wherein:

Y^1 is independently O, S, $N(R^x)$, $N(O)(R^x)$, $N(OR^x)$, $N(O)(OR^x)$, or $N(N(R^x)(R^x))$;

Y^2 is independently a bond, O, $N(R^x)$, $N(O)(R^x)$, $N(OR^x)$, $N(O)(OR^x)$, $N(N(R^x)(R^x))$, -S(O)- (sulfoxide), $-S(O)_2-$ (sulfone), -S- (sulfide), or -S-S- (disulfide);

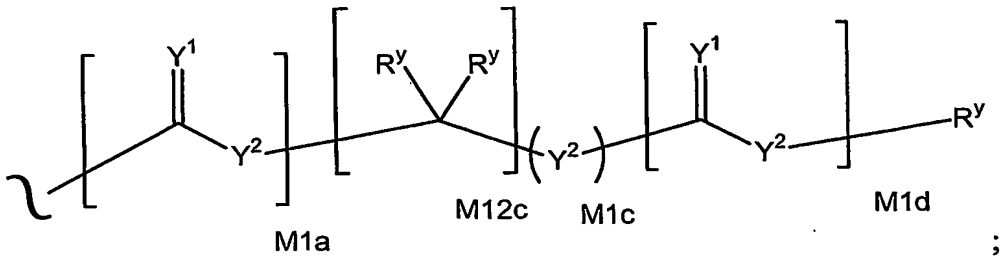
M2 is 0, 1 or 2;

M12a is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12;

M12b is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12;

R^y is independently H, alkyl, substituted alkyl, aryl, substituted aryl, or a protecting group, or where taken together at a carbon atom, two vicinal R^y groups form a carbocycle or a heterocycle; and

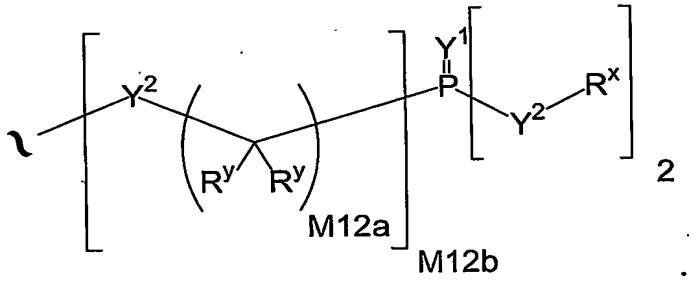
R^x is independently H, alkyl, substituted alkyl, aryl, substituted aryl, or a protecting group, or the formula:



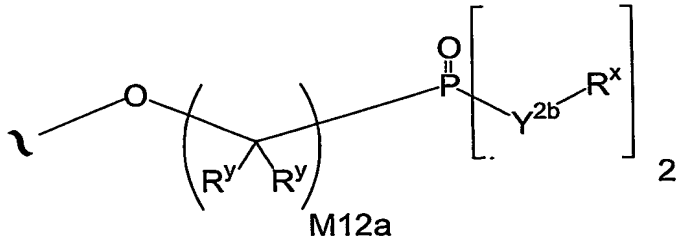
;

where M1a, M1c, and M1d are independently 0 or 1, and M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12.

18. The compound of claim 17 wherein phosphonate group has the structure:

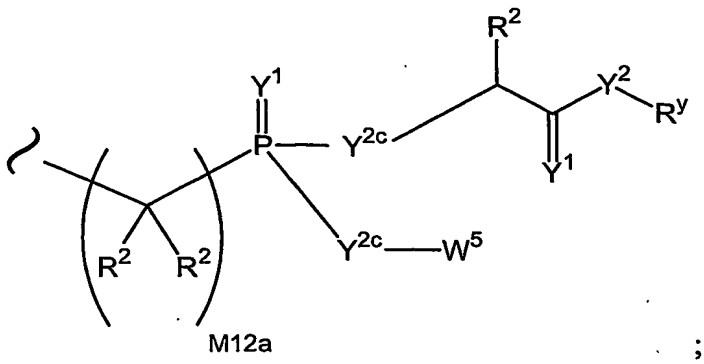


19. The compound of claim 18 wherein phosphonate group has the structure:



where Y^{2b} is O or N(R^x).

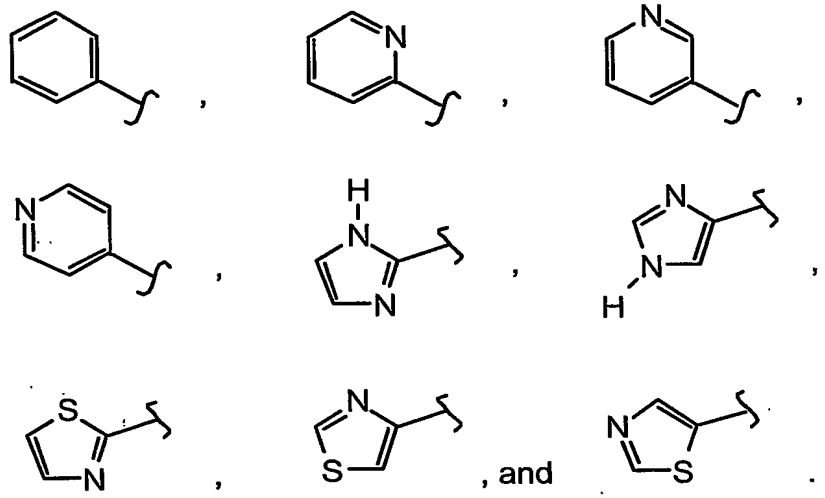
20. The compound of claim 18 wherein phosphonate group has the structure:



M12a ;

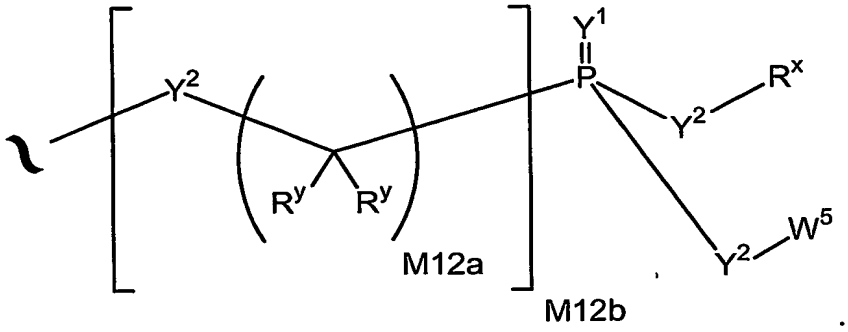
where W^5 is a carbocycle, and Y^{2c} is O, N(R^y) or S.

21. The compound of claim 20 wherein W^5 is selected from the structures:

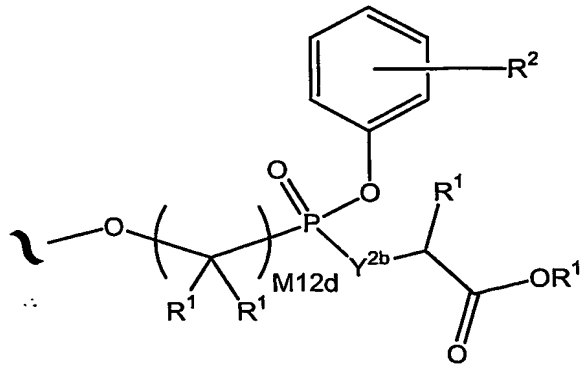


, and .

22. The compound of claim 17 wherein phosphonate group has the structure:

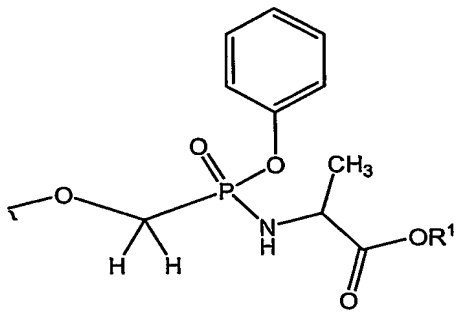


23. The compound of claim 22 wherein phosphonate group has the structure:

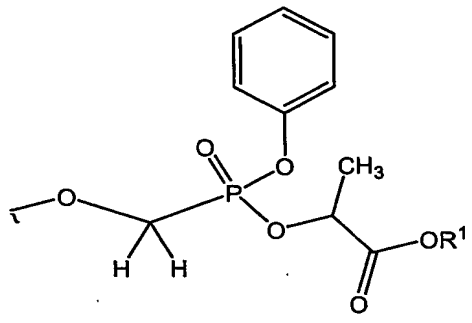


wherein Y^{2b} is O or N(R^x); M12d is 1, 2, 3, 4, 5, 6, 7 or 8; R^1 is H or C_1–C_6 alkyl; and the phenyl carbocycle is substituted with 0 to 3 R^2 groups where R^2 is C_1–C_6 alkyl or substituted alkyl.

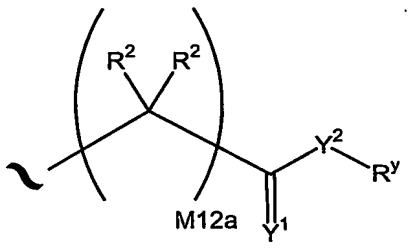
24. The compound of claim 23 wherein phosphonate group has the structure:



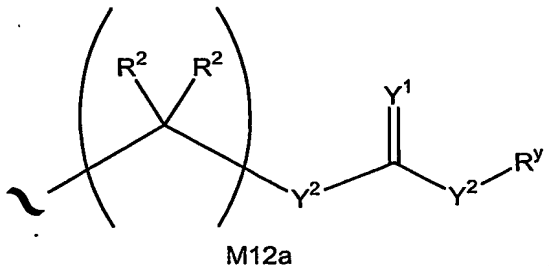
or



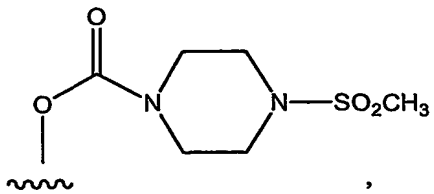
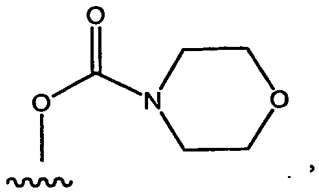
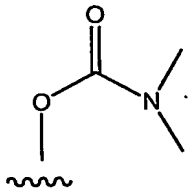
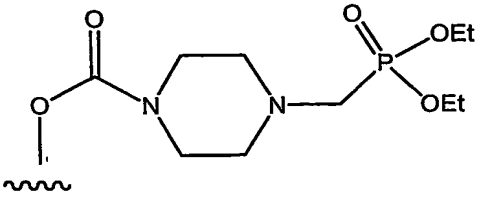
25. The compound of claim 17 wherein R^x is selected from the structures:



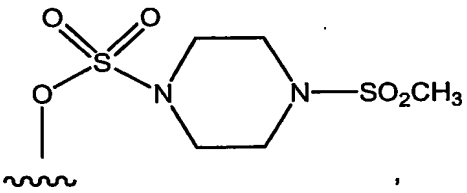
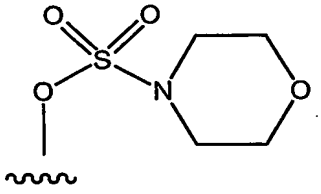
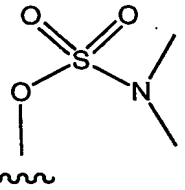
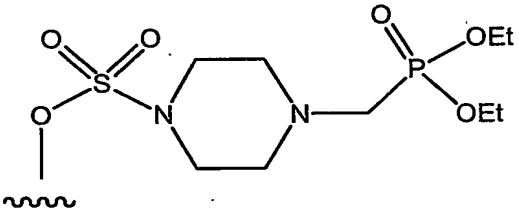
and



26. The compound of claim 25 wherein X^2 is CR^2 and R^2 is selected from the structures:

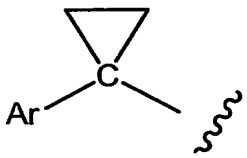
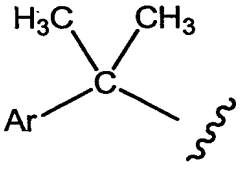



and


27. The compound of claim 25 wherein X^2 is CR^2 and R^2 is selected from the structures:

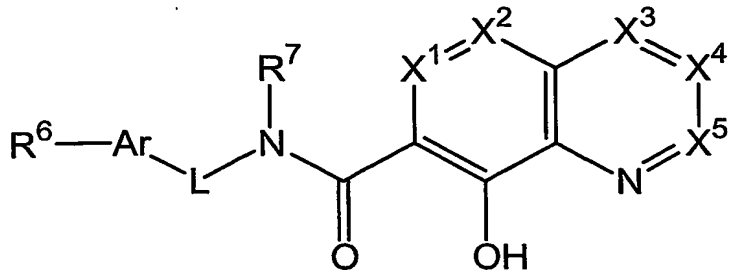



and


28. A compound of claim 1 wherein X^2 is CR^2 and R^2 comprises a phosphonate prodrug moiety.

29. The compound of claim 1 wherein Ar-L is selected from the structures:


and


30. A compound having the formula:



or a pharmaceutically acceptable salt thereof, and including enol and tautomeric resonance isomers;

wherein:

X^1 is CR^1, NR, or N;

X^2 is CR^2, NR, or N;

X^3 is CR^3, NR, or N;

X^4 is CR^4, NR, or N;

X^5 is CR^5, NR, or N;

at least one of X^1, X^2, X^3, X^4, and X^5 is NR or N;

R^1, R^2, R^3, R^4, R^5, R^6, and R^7 are independently selected from H, F, Cl, Br, I, OH, amino ($-NH_2$), ammonium ($-NH_3^+$), alkylamino, dialkylamino, trialkylammonium, C_1–C_8 alkyl, C_1–C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1–C_8 alkylsulfonate, C_1–C_8 alkylamino, 4-dialkylaminopyridinium, C_1–C_8 alkylhydroxyl, C_1–C_8 alkylthiol, alkylsulfone ($-SO_2R$), arylsulfone ($-SO_2Ar$), arylsulfoxide ($-SOAr$), arylthio ($-SAr$), sulfonamide ($-SO_2NR_2$), alkylsulfoxide ($-SOR$), formyl ($-CHO$), ester ($-C(=O)OR$), amido ($-C(=O)NR_2$), 5-7 membered ring lactam, 5-7 membered ring lactone, nitrile ($-CN$), azido ($-N_3$), nitro ($-NO_2$), C_1–C_8 alkoxy ($-OR$), C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, phosphonate, phosphate, polyethyleneoxy, and a prodrug moiety; or when X^1 is CR^1 and when X^2 is CR^2, then CR^1 and CR^2 together may form a ring; when X^3 is CR^3 and when X^4 is CR^4, then CR^3 and CR^4 together may form a ring; or when. X^4 is CR^4 and X^5 is CR^5, then CR^4 and CR^5 together may form a ring; wherein the ring is 5, 6, or 7-membered;

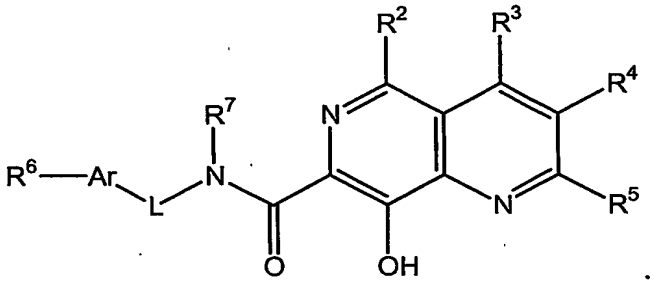
R is independently selected from H, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl;

L is selected from a bond, O, S, NR, N–OR, C_1–C_{12} alkylene, C_1–C_{12} substituted alkylene, C_2–C_{12} alkenylene, C_2–C_{12} substituted alkenylene, C_2–C_{12} alkynylene, C_2–C_{12} substituted alkynylene, C(=O)NH, C(=O), $S(=O)_2$, $C(=O)NH(CH_2)_n$, and $(CH_2CH_2O)_n$, where n may be 1, 2, 3, 4, 5, or 6; and

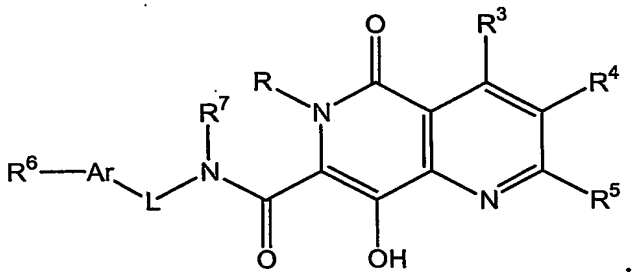
Ar is covalently attached to L and to one or more R^6 and Ar is selected from C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl;

where at least one of R, R^1, R^2, R^3, R^4, R^5, R^6, and R^7 comprises a phosphonate group.

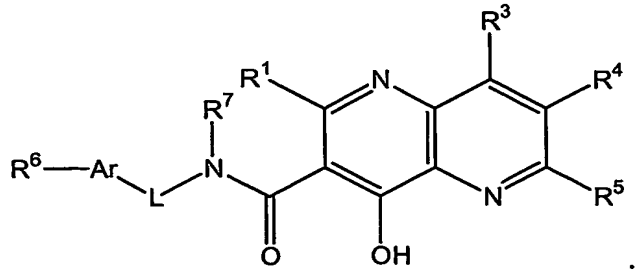
31. A compound according to claim 30 having the formula:



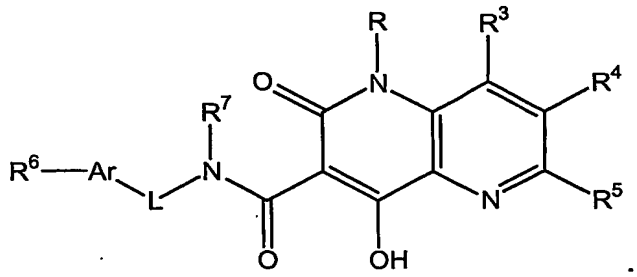
32. A compound according to claim 30 having the formula:



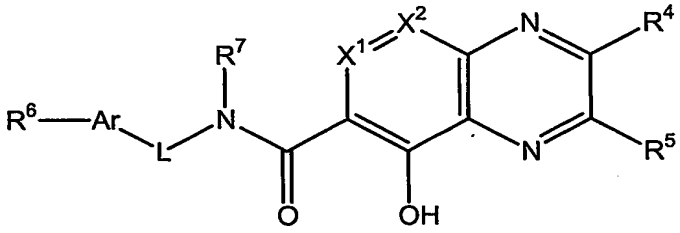
33. A compound according to claim 30 having the formula:



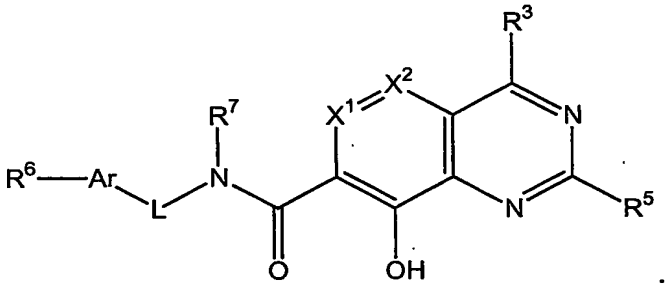
34. A compound according to claim 30 having the formula:



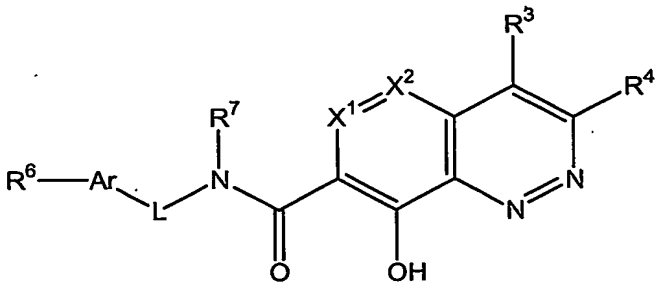
35. A compound according to claim 30 having the formula:



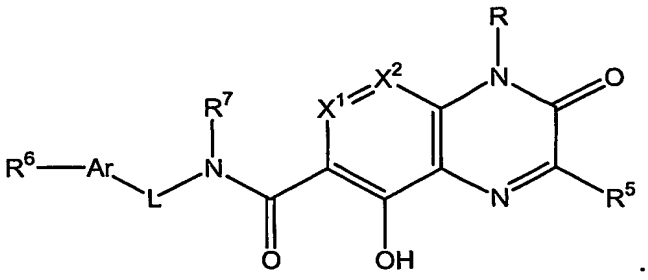
36. A compound according to claim 30 having the formula:



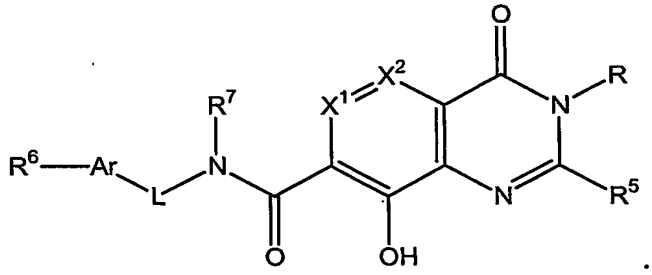
37. A compound according to claim 30 having the formula:



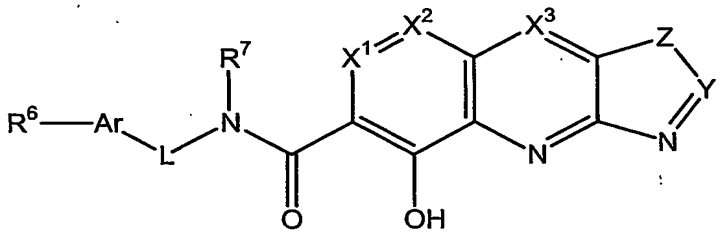
38. A compound according to claim 30 having the formula:



39. A compound according to claim 30 having the formula:



40. A compound according to claim 30 having the formula:



wherein

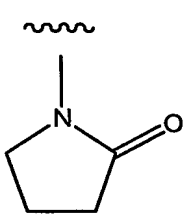
Y is CR^5, NR or N; and

Z is selected from O, S, NR, CR_2, CROR, CROC(=O)R, C(=O), C(=S), CRSR, $C(=NR_2)$, $C=CR_2$, $CR_2–CR_2$, CR=CR, NR–CR_2, N=CR, N=N, SO_2–NR, $C(=O)CR_2$, $S(=O)CR_2$, SO_2CR_2, C(=O)NR, $CR_2–CR_2–CR_2$, CR=CR–CR_2, CRC(=O)NR, $CR_2SO_2CR_2$, CR_2SO_2NR, CRC(=S)NR, CR=N–CR_2, CR=N–NR, or N=CR–NR.

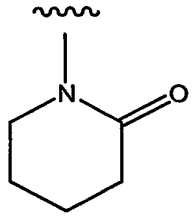
41. The compound of claim 30 wherein substituted alkylene, substituted alkyenylene, substituted alkynylene, substituted aryl, and substituted heteroaryl are independently substituted with one or more substituents selected from F, Cl, Br, I, OH, amino ($–NH_2$), ammonium ($–NH_3^+$), alkylamino, dialkylamino, trialkylammonium, $C_1–C_8$ alkyl, $C_1–C_8$ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring

sultam, C_1–C_8 alkylsulfonate, C_1–C_8 alkylamino, 4-dialkylaminopyridinium, C_1–C_8 alkylhydroxyl, C_1–C_8 alkylthiol, alkylsulfone (–SO_2R), arylsulfone (–SO_2Ar), arylsulfoxide (–SOAr), arylthio (–SAr), sulfonamide (–SO_2NR_2), alkylsulfoxide (–SOR), ester (–C(=O)OR), amido (–C(=O)NR_2), 5-7 membered ring lactam, 5-7 membered ring lactone, nitrile (–CN), azido (–N_3), nitro (–NO_2), C_1–C_8 alkoxy (–OR), C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, phosphonate, phosphate, polyethyleneoxy, and a prodrug moiety.

42. A compound of claim 30 wherein X^2 is CR^2 and R^2 is selected from H, OH, OC(=O)OR, OC(=O)NR_2, OC(=O)R, OSO_2NR_2 (sulfamate), NR_2, $NRSO_2R$, SR, S(O)R, SO_2R or SO_2NR_2 (sulfonamide), lactam having the structures:

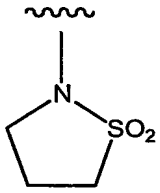


and

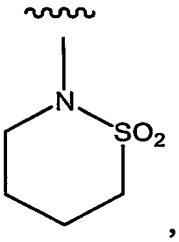


,

sultam having the structures:



and



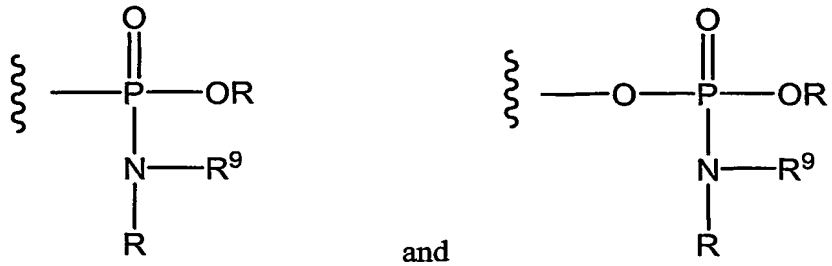
,

and a prodrug moiety.

43. The compound of claim 30 wherein L is CH_2 and Ar is substituted phenyl.

44. The compound of claim 30 where L is CH_2 and Ar is 4-fluorophenyl.

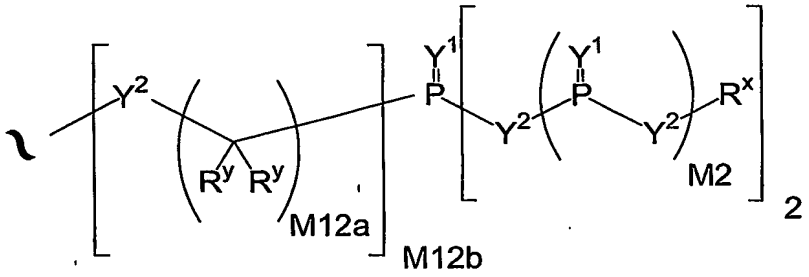
45. The compound of claim 30 wherein at least one of R^1, R^2, R^3, R^4, R^5, R^6, and R^7 comprise a prodrug moiety selected from the structures:



and

wherein R^9 is comprised of an ester, an amide, or a carbamate.

46. The compound of claim 30 wherein the phosphonate group has the structure:



wherein:

Y^1 is independently O, S, $N(R^x)$, $N(O)(R^x)$, $N(OR^x)$, $N(O)(OR^x)$, or $N(N(R^x)(R^x))$;

Y^2 is independently a bond, O, $N(R^x)$, $N(O)(R^x)$, $N(OR^x)$, $N(O)(OR^x)$, $N(N(R^x)(R^x))$, -S(O)- (sulfoxide), $-S(O)_2-$ (sulfone), -S- (sulfide), or -S-S- (disulfide);

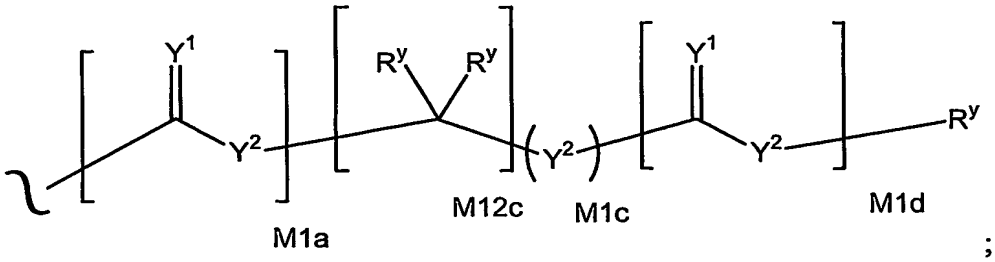
M2 is 0, 1 or 2;

M12a is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12;

M12b is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12;

R^y is independently H, alkyl, substituted alkyl, aryl, substituted aryl, or a protecting group, or where taken together at a carbon atom, two vicinal R^y groups form a carbocycle or a heterocycle; and

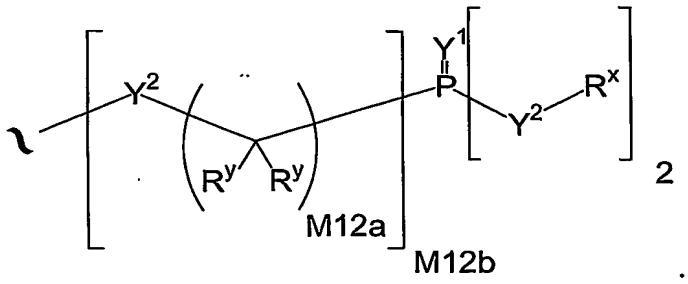
R^x is independently H, alkyl, substituted alkyl, aryl, substituted aryl, or a protecting group, or the formula:



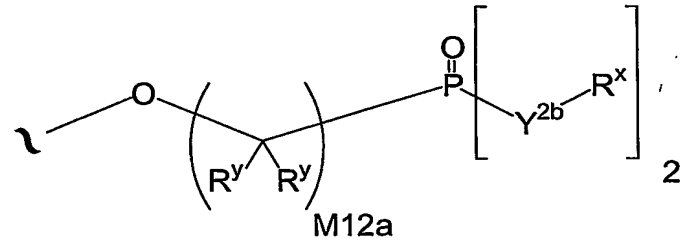
;

where M1a, M1c, and M1d are independently 0 or 1, and M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12.

47. The compound of claim 46 wherein phosphonate group has the structure:

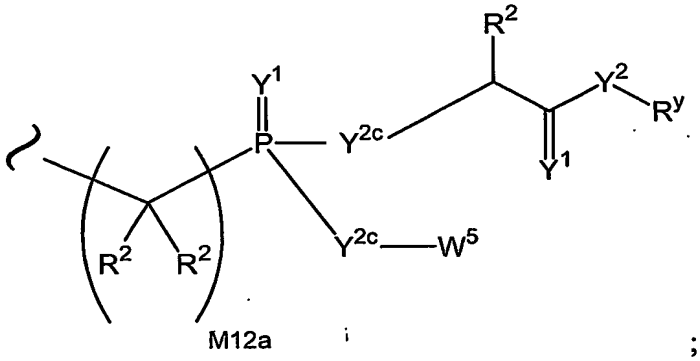


48. The compound of claim 47 wherein phosphonate group has the structure:



where Y^{2b} is O or $N(R^x)$.

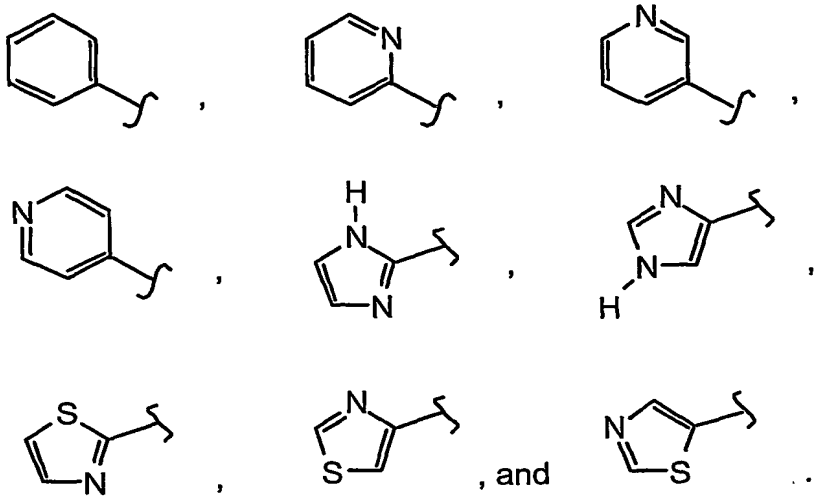
49. The compound of claim 47 wherein phosphonate group has the structure:



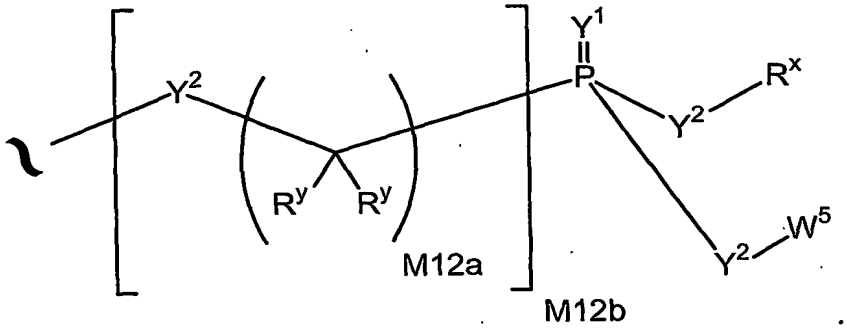
;

where W^5 is a carbocycle, and Y^{2c} is O, $N(R^y)$ or S.

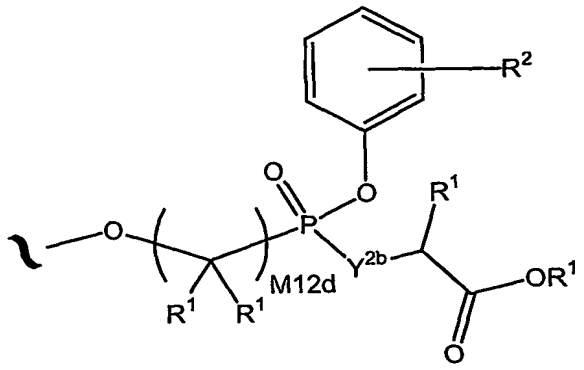
50. The compound of claim 49 wherein W^5 is selected from the structures:



51. The compound of claim 46 wherein phosphonate group has the structure:

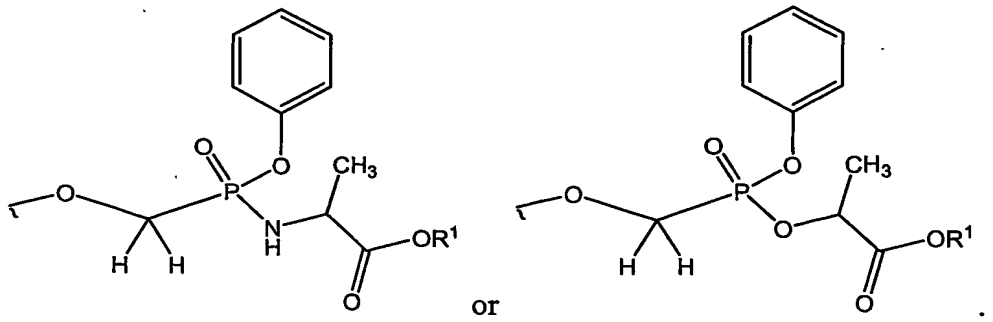


52. The compound of claim 51 wherein phosphonate group has the structure:



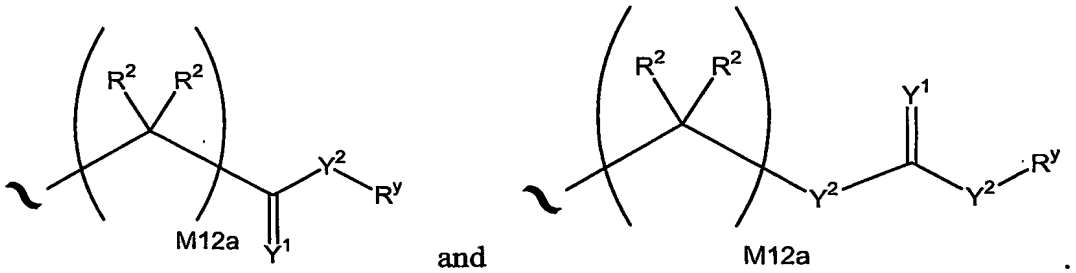
wherein Y^{2b} is O or N(R^x); M12d is 1, 2, 3, 4, 5, 6, 7 or 8; R^1 is H or C_1–C_6 alkyl; and the phenyl carbocycle is substituted with 0 to 3 R^2 groups where R^2 is C_1–C_6 alkyl or substituted alkyl.

53. The compound of claim 52 wherein phosphonate group has the structure:



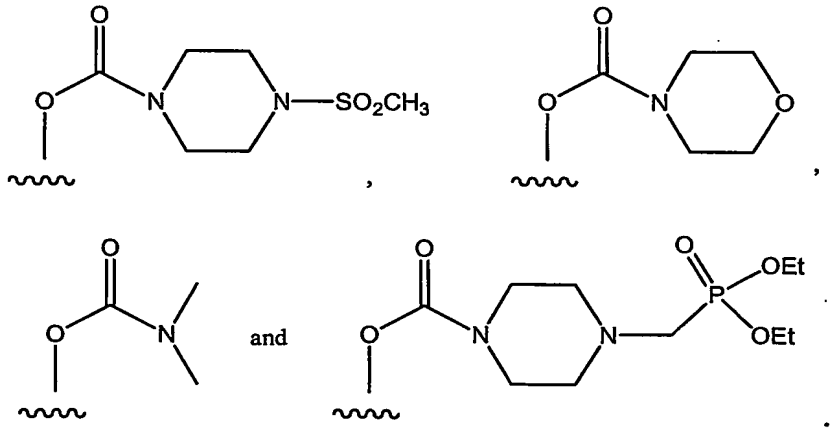
or

54. The compound of claim 46 wherein R^x is selected from the structures:



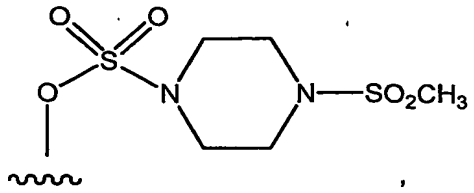
and

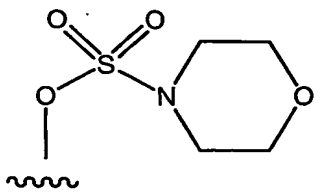
55. The compound of claim 54 wherein X^2 is CR^2 and R^2 is selected from the structures:

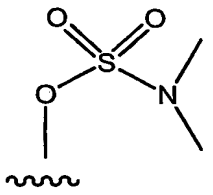


and

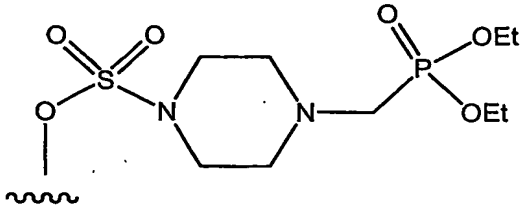
56. The compound of claim 54 wherein X^2 is CR^2 and R^2 is selected from the structures:





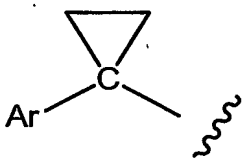


and

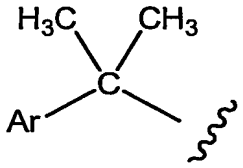


57. A compound of claim 30 wherein X^2 is CR^2 and R^2 comprises a phosphonate prodrug moiety.

58. The compound of claim 31 wherein Ar-L is selected from the structures:



and



59. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable carrier.

60. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 in combination with a therapeutically effective amount of an AIDS treatment agent selected from:

(1) an AIDS antiviral agent,

(2) an anti-infective agent, and

(3) an immunomodulator.

61. The composition of claim 60 wherein the antiviral agent is an HIV protease inhibitor.

62. A pharmaceutical composition made by combining the compound of claim 1 and a pharmaceutically acceptable carrier.

63. A process for making a pharmaceutical composition comprising combining a compound of claim 1 and a pharmaceutically acceptable carrier.

64. A method of inhibiting HIV integrase, comprising the administration to a mammal in need of such treatment of a therapeutically effective amount of a compound of claim 1.

65. A method of treating infection by HIV, or of treating AIDS or ARC, comprising administration to a mammal in need of such treatment of a therapeutically effective amount of a compound of claim 1.